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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,580	11/14/2003	Paul Wentworth	1361.027US1	1792

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/714,580	WENTWORTH ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III in the reply filed on November 9, 2005 is acknowledged. The traversal is on the ground(s) that a search of all three groups would not be unduly burdensome. This is not found persuasive because the inventions are distinct and unrelated, each from the other because of the reasons previously provided. Inventions are unrelated since it has been shown that they are not disclosed as capable of use together and that they have different modes of operation, different functions, or different effects. Therefore, the inventions are patentably distinct.

Applicants' argue that there would be no serious burden on the Examiner to search for the other groups. However, in the instant case these inventions are unrelated and distinct. The methods are distinct as claimed because they are drawn to measuring or performing different activities. Furthermore the distinct steps and products require separate and distinct searches. The groups have a separate status in the art as shown by their different classification. As such, it would be burdensome to search the inventions of groups together. Furthermore, a search for the invention of the groups would not be coextensive because a search indicating the process of one is novel or unobvious would not extend to a holding that the process of the other is novel or unobvious. Because of the different classifications of each group based upon the distinct method steps, a serious burden is imposed on the examiner to perform a complete search of the defined areas in both the patent and non-patent literature. Therefore, because of the reasons given above, the restriction set forth is proper and

not to restrict would impose a serious burden on the examination of this application, contrary to applicants' assertions. The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 40-47 of this application. The instant claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen. However, none of the provisional applications, for which priority is claimed 60/232/702, 60/235,475, 60/426,245, and 60/315,906 and PCT/US01/29165 teach a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen. Thus, there was no conception of a method for generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen. Therefore, priority cannot be granted to 60/232/702, 60/235,475, 60/426,245, and 60/315,906 and PCT/US01/29165 since what is now claimed, has not been previously recited in the other applications.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 40-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

The claims are so broad that they encompass the detection of every type of microbe, however applicants have not described such a method. The instant specification fails to provide a method where all microbial growth will be inhibited. The specification fails to teach that every type of microbe can be used within the claimed method. There is no teaching that growth will be inhibited in parasites, viruses, fungi, yeasts and bacteria. The specification teaches the bactericidal activity of the antibody and source of singlet oxygen within an in vitro assay. Moreover, example IV teaches said activity towards *Salmonella*. Wherein the inhibition of growth occurred during the *in*

vitro portion. There is no written description of any method steps which teach such broadly claimed methods. There are no examples that teach the inhibition of each and every type of microorganism. The claims fail to recite the necessary method steps. There are no data showing that the growth will be inhibited in every microbe. The specification does not provide a substantive description that the claimed method is capable of inhibiting growth in all microbial species. This demonstration is required for the skilled artisan to be able to use the claimed method for its intended purpose. The generic statements drawn to the method do not provide ample written description for the method. Furthermore, the statements the method being capable of detecting viruses, parasites and fungi does not sufficiently provide ample written description since only bacterial growth is inhibited.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 40 is a broad generic with respect all possible microbes encompassed by the claims. The possible structural variations are limitless to any class of microorganisms. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of anything other than bacteria. The specification is void of any microorganism which could be used within the instantly claimed method. The specification is limited to bacteria. The written description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir.

1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention and the claims are rejected.

5. Claims 40-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of the claims is drawn to a method of generating a reactive oxygen species to inhibit the growth of a microbe, however the recited steps within the method comprise only a contacting step. There is no correlation step which correlates the generation a reactive oxygen species which inhibits the growth of a microbe to the contacting step. Therefore, the goal of the preamble is not commensurate with the steps of the method that are drawn to inhibiting microbial growth.

6. Claims 40-47 are rejected as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MEP. § 2172.01. The claims lack essential steps and reagents such as the use of light which generates the oxidation of the products. Furthermore, the claims lack a correlation step that correlates the

contacted antibody and source of singlet oxygen to the inhibition of microbial growth as previously discussed. Therefore appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 40-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Devanathan et al. The claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen. The dependant claims are drawn to specific sources for the singlet oxygen.

Devanathan et al., teach readily available fluorescein isothiocyante-conjugated antibodies which can be easily converted into targeted agents for antibacterial therapy. The prior art teaches that for photodynamic killing of microorganism, light, oxygen and absorbing dyes called photodynamic sensitizers are essential (page 2980). In an attempt to direct the sensitizer to the target, one can use antibody-photodynamic sensitizer conjugates (page 2980). These have been useful as therapeutic agents for the selective destruction of microorganisms wherein the photodynamic sensitizer must not only be phototoxic, but also selective (page 2980). The authors disclose that the more halogenated fluorescein rings are, the more efficient photodynamic sensitizers

they become (page 2980). The authors teach that Rose Bengal is one of these more efficient photodynamic sensitizers (page 2980). Devanathan et al., teach activating the photosensitizing activity of a fluoresceinated antibody that binds to rabbit IgG antibodies (page 2980). The mixing of this diiodofluorescein photodynamic sensitizer-antibody conjugate with rabbit anti-*Escherichia coli* IgG antibody and illuminating in a mixture of *E. coli* and *Salmonella typhimurium* results in the selective inactivation of the *E. coli* bacteria (page 2980). Similar selectivity is observed with Rose Bengal-sensitized inactivation of strains of *S. typhimurium* (page 2983). The photoactive diiodofluorescein generates singlet oxygen when illuminated and the singlet oxygen is a potent cytotoxicant to *Salmonella* and *E. coli* (page 2983). Thus the art teaches sensitizer molecules as the source of the singlet oxygen. Therefore the authors believe that the diiodofluorescein-antibody inactivates the bacteria by the generation of the cytotoxic singlet oxygen (page 2983). Therefore the art teaches that the sensitizer molecule is attached to the antibody, just as required by the claims.

Therefore, Devanathan et al., teach a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen is a sensitizer molecule just as required by the claims.

8. Claims 40-43 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Berthlaume et al. The claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen. The dependant claims are drawn to specific sources for the singlet oxygen, and the types of antibodies.

Berthlaume et al., teach antibody-targeted photolysis of bacteria *in vivo*. The authors have developed an antibody-targeted photolysis method which uses antibody bound photosensitizers which are toxic only upon activation of light (page 703). The authors teach that bacterial killing *in vitro* using tin (IV) chlorine e_6 as the photosensitizer was shown to be highly efficient in the production of singlet oxygen and other short-lived species (page 703). Thus the art teaches sensitizer molecules as the source of the singlet oxygen. The results of this study show that specific tin (IV) chlorine e_6-monoclonal antibody conjugates directed against *P. aeruginosa* can specifically kill more than 75% of the bacteria (page 703). Therefore the art teaches that the sensitizer molecule is attached to the antibody, just as required by the claims. Berthlaume et al., teach transport studies of antibody fragments have shown improved and rapid infiltration of the selected target sites (page 705).

Therefore, Berthlaume et al., teach a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody or antibody fragment that can bind to the microbe and (ii) a source of singlet oxygen is a sensitizer molecule just as required by the claims.

9. Claims 40-42 and 44-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Wentworth et al., in light of the Scripps Press Release of November 14, 2002. At the outset, the examiner sets forth that M.P.E.P. section 2131.01 entitled Multiple Reference 35 U.S.C. 102 Rejections states that a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra reference is cited to show that a characteristic not disclosed in the reference is inherent.

The claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a microbe comprising contacting the microbe with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen. The dependant claims are drawn to specific sources for the singlet oxygen, the types of antibodies and the reactive species generated.

Wentworth et al., (PNAS, 2000) teach antibodies have the intrinsic capacity to destroy antigens. Antibodies have the capacity to convert molecular oxygen into hydrogen peroxide, thereby effectively linking recognition and killing events (page 10,930). The authors disclosed this capability with whole antibodies and $F(ab')_2$ fragments (see the materials and methods section). The sensitization and quenching assays teach a solution of horse IgG antibody and sensitizer molecule, hematopophyrin were placed in proximity to a strip of light and the concentration of hydrogen peroxide produced was determined (page 10,930). Thus the art teaches hematopophyrin as a sensitizer molecule and source of the singlet oxygen. Wentworth et al., teach that superoxide anion radicals are the direct precursor of hydrogen peroxide and the toxic derivatives it spawns, such as hydroxyl radials (HO*). Thus the art teaches that the

reactive oxygen species generated is a superoxide radical, hydroxyl radical or hydrogen peroxide, just as required by the claims. It is noted that the art is silent with respect to the generation of an ozone as a reactive oxygen species.

However, the Scripps Press Release inherently teaches the production of ozone by antibodies during bacterial killing has played an hitherto unknown role in immune protection (Scripps Press Release). The ozone is part of a previously unrecognized killing mechanism that enhances the defensive role of antibodies by allowing them to subject pathogens to hydrogen peroxide and participate directly in their killing. Antibodies produce the chemical oxidant hydrogen peroxide which is lethal to bacterial cells because it pokes holes in their cell walls, bursting the cells and killing them. The antibodies reduce singlet oxygen and produce ozone as a side product. The authors state that all antibodies have the ability to do this. Therefore the generation of hydrogen peroxide and ozone as a side product, are inherent abilities that antibodies have. Thus, the Scripps Press Release teach that inherently, antibodies will generate ozone as a reactive species which will inhibit the growth of a bacterial microbe, just as required by the claims.

Prior Art

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Srinivasan et al, (1978) teach the Rose Bengal as being the source of singlet oxygen, the mechanism of singlet oxygen formation and the role of superoxide in reactions attributed to singlet oxygen. Wentworth et al., (Science, 2001)

teach antibodies, regardless of their source of antigenic specificity generate hydrogen peroxide (H_2O_2) from $^1O_2$*, a singlet molecular oxygen, thereby potentially aligning recognition and killing within the same molecule.

Conclusion

11. No claims allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
January 30, 2006

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